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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/360,685	07/26/1999	ANTONELLO COVACCI	CHIR-0157	4520

27476 7590 06/15/2004

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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/360,685	COVACCI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *40,41 and 127* is/are allowed.

6)☒ Claim(s) *45, 49, 54, 56, 57, 59, 62, 63, 68, 70, 78, 80, 81, 88, 123-126, 128 and 140* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/256,848.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Sequence search reports (2 pages)

Continuation of Disposition of Claims: Claims pending in the application are 40,41,45,49,54,56,57,59,62,63,68,70,78,80,81,88,123-126,128 and 140.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 03/25/04 has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 02/25/04 in response to the final Office Action mailed 11/25/03.

Status of Claims

3) Claims 45, 47, 54, 56, 57, 62, 63, 70, 78, 81, 88, 123-127 and 140 have been amended via the amendment filed 02/25/04.

Claims 75, 76, 82-87, 89-122 and 129-139 have been canceled via the amendment filed 02/25/04.

Claims 40, 41, 45, 47, 54, 56, 57, 59, 62, 63, 68, 70, 78, 80, 81, 88, 123-128 and 140 are pending and are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Specification - New Matter

6) The first paragraph to the specification amended via the amendment filed 07/25/02 is objected to under 35 U.S.C. § 132, because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The recitation: 'the entire contents of each application is incorporated by reference herein' is new matter. For the incorporation by reference to be effective as a proper safeguard against the omission of a

portion of a prior application, the incorporation by reference statement must be included in the specification-as-filed, or transmittal letter-as-filed, or in an amendment specifically referred to in an oath or declaration executing the application. An incorporation by reference statement added after an application's filing date is not effective because no new matter can be added to an application after its filing date. See 35 U.S.C § 132(a). If an incorporation by reference statement is included in an amendment to the specification to add a benefit claim after the filing date of the application, the amendment would not be proper. In the instant application, via the transmittal letter filed 07/26/199 only the application PCT/EP93/00472, filed 03/02/1993, was incorporated by reference but not PCT/EP93/00158 and the Italian application FI92A000052, filed 03/02/1992. When a benefit claim is submitted after the filing of an application, the reference to the prior application cannot include an incorporation by reference statement of the prior application. See *Dart Indus. v. Banner*, 636 F.2d 684, 207 USPQ 273 (C.A.D.C 1980).

Rejection(s) Moot

7) The rejection of claim 76 made in paragraph 17 of the Office Action mailed 05/20/03 (paper no. 40) and maintained in paragraph 21 of the Office Action mailed 11/25/03 under 35 U.S.C. § 102(e) as being anticipated by Cover *et al.* (US 5,403,924), is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 76 made in paragraph 22 of the Office Action mailed 11/25/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

9) The rejection of claims 93 and 130 made in paragraph 23 of the Office Action mailed 11/25/03 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of the claim.

10) The rejection of claims 93 and 130 made in paragraph 24 of the Office Action mailed 11/25/03 under 35 U.S.C. § 102(e) as being anticipated by Cover *et al.* (US 5,403,924 - already of record) ('924), is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

11) The rejection of claims 81 and 88 made in paragraph 25 of the Office Action mailed 11/25/03 under 35 U.S.C. § 102(b) as being anticipated by Peterson *et al.* (*Nature* 354: 369-373, 1991,

already of record), is withdrawn in light of Applicants' amendment to the base claim. A modified rejection is made herebelow.

12) The rejection of claims 45, 47, 54, 56, 62, 68, 78, 81, 88 and 123-125 made in paragraph 17 of the Office Action mailed 05/20/03 and maintained in paragraph 21 of the Office Action mailed 11/25/03 under 35 U.S.C. § 102(e) as being anticipated by Cover *et al.* (US 5,403,924), is withdrawn in light of Applicants' amendments to the claims and/or the base claim(s)

Rejection(s) under 35 U.S.C. § 112, First Paragraph

13) Claims 45, 47, 54, 56, 62, 68, 78, 81 and 88 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Instant claims include the new limitation: 'amino acids 750-977 of the' amino acid sequence of' SEQ ID NO: 5. Applicants point to Figure 3C of the Italian priority document, FI92A 000052, which allegedly is incorporated by reference into the present specification. However, there appears to be no descriptive support either in the Italian document, FI92A 000052, or in the instant specification for this limitation. What is depicted in Figure 3C of the priority document is described in claims 1-3 of the priority document as the 'protein extracted from cytotoxic strains' of *Helicobacter pylori* 'having a molecular weight of about 130 kDa'. This 'protein' has amino acids 1-228, as opposed to a polypeptide comprising at least five or at least ten contiguous amino acids from amino acids 750-977 of the amino acid sequence of SEQ ID NO: 5 wherein the polypeptide comprises SEQ ID NO: 10 or six contiguous asparagine residues. Figure 3C does not depict the polypeptide of SEQ ID NO: 5. Figure 3C of the priority document is not described as depicting a polypeptide that is separable from the instantly recited SEQ ID NO: 5. Figure 3C of the priority document does not identify SEQ ID NO: 10 or six contiguous asparagine residues within the depicted amino acid sequence either by underlining or by boxing as in Figure 4C of the instant application. An at least ten and five amino acid-long fragments from amino acids 750-977 of the amino acid sequence of SEQ ID NO: 5 are not described in the instant application and in the Italian priority document. Therefore, the limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also,

adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or point to specific pages and line numbers in the originally filed specification where support for such recitations can be found.

14) Claims 123-125 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Instant claims include the new limitation: 'nucleotides 2782-3466 of the' nucleotide sequence of' SEQ ID NO: 4. Applicants point to Figure 3B of Applicants' Italian priority document, allegedly incorporated by reference into the present specification. However, there appears to be no descriptive support in the priority document or in the instant specification for this limitation. What is depicted in Figure 3B of the priority document is described in claims 1-3 of the priority document, FI92A 000052, as the 'gene' that expresses the 'protein' from cytotoxic strains' of *Helicobacter pylori* 'having a molecular weight of about 130 kDa' having the amino acid sequence containing amino acids 1-228. This 'gene' has the nucleotides 1-699, as opposed to at least fifteen, thirty or forty five nucleotides of nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO: 4. Figure 3B does not depict the nucleotide sequence of SEQ ID NO: 4. Figure 3B of the priority document is not described as depicting a nucleotide sequence that is separable from the instantly recited SEQ ID NO: 4. An at least 15, 30 and 45 nucleotide-long fragments from nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO: 4 are not described in the instant application and in the Italian priority document. Therefore, the limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or point to specific pages and line numbers in the originally filed specification where support for such recitations can be found.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

15) Claims 57, 59, 63, 70, 80, 126, 128 and 140 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 57 is indefinite, confusing and/or internally inconsistent in the recitation: 'at least ten contiguous amino acids of the amino acid sequence of SEQ ID NO: 5, wherein said polypeptide includes ..... SEQ ID NO: 9'. The minimum length requirement of the claimed polypeptide is ten contiguous amino acids of the amino acid sequence of SEQ ID NO: 5, and it is required to include SEQ ID NO: 9. However, SEQ ID NO: 9 is longer than ten contiguous amino acids in length. It is unclear how a longer than ten contiguous amino acid-long polypeptide can be contained in a ten contiguous amino acid-long polypeptide.

(b) Claims 57, 59, 63 and 140 are vague and confusing in the limitation: 'polypeptide comprises at least ..... contiguous amino acids of the *Helicobacter pylori* heat shock protein having the amino acid sequence of SEQ ID NO: 6'. It is unclear whether the second polypeptide is the one which has the amino acid sequence of SEQ ID NO: 6, or whether SEQ ID NO: 6 represents the amino acid sequence of SEQ ID NO: 6. If latter is intended, it is suggested that Applicants replace the last line of claim 59 with --*pylori* heat shock protein, said protein having the amino acid sequence of SEQ ID NO: 6--. Analogous suggestion applies to claims 57, 63 and 140.

(c) Analogous rejection as set forth above in item (b) applies to claims 70, 80 and 126.

(d) Claim 57 is vague, indefinite and/or incorrect in the recitation: 'andan' (see the end of line 6).

(e) Claims 59 and 128, which depend directly or indirectly from claim 57 or 126, are also rejected as being indefinite because of the vagueness or indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

16) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by

> the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

17) Claims 81 and 88 are rejected under 35 U.S.C. § 102(b) as being anticipated by Peterson *et al.* (*Nature* 354: 369-373, 1991, already of record).

Instant claims are afforded the filing date of the instant invention since the newly added limitation 'amino acids 750-977 of the ' amino acid sequence of SEQ ID NO: 5 does not have support in the priority document or prior applications.

Peterson *et al.* taught a purified recombinant polypeptide comprising the amino acid sequence of SEQ ID NO: 10, EPIYA. See abstract; and the sequence search report attached to the Office Action mailed 05/20/03. The prior art polypeptide is structurally identical to the instantly claimed polypeptide, irrespective of how it is isolated. Peterson's polypeptide is the same as Applicants' polypeptide based upon the fact that every structural characteristic overlapping in Paterson's and Applicants' disclosure are the same.

The recitation 'recombinant' in claim 88 is viewed as a process limitation in a product claim. It should be noted that when claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the isolation process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art polypeptide differs from that of the instantly claimed polypeptide.

Claims 81 and 88 are anticipated by Peterson *et al.*

18) Claims 81 and 88 are rejected under 35 U.S.C. § 102(b) as being anticipated by Guntaka *et al.* (*Biochem. Biophys. Res. Commun.* 182: 412-419, 1992).

Guntaka *et al.* taught a recombinant polypeptide comprising at least five contiguous amino

acids from amino acids 750-977 of the instantly recited amino acid sequence of SEQ ID NO: 5, wherein the polypeptide includes the six contiguous asparagine residues, NNNNNNGL. See the attached sequence alignment report; Figure 3, Materials and Methods, and Results of Guntaka *et al.*

Claims 81 and 88 are anticipated by Guntaka *et al.*

19) Claims 123-126 and 128 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924).

Cover *et al.* ('924) disclosed an isolated polypeptide, ValGluGlnAlaLeuAlaAspLeuLysAsnPheSerLysGluGlnLeuAlaGlnGlnAlaGlnLysAsnGluSer, encoded by 75 contiguous nucleotides from nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO: 4 (see the last two lines in columns 31 and 32 and line 1 in columns 33 and 34 of the '924 patent). See the attached sequence search report. The prior art polypeptide is long enough to serve as an antigen having the amino acid sequence of SEQ ID NO: 5.

The limitation 'recombinant' in claim 128 is viewed as a process limitation in a product claim. It should be noted that when claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the isolation process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art polypeptide differs from that of the instantly claimed polypeptide.

Claims 123-126 and 128 are anticipated by Cover *et al.* ('924).

20) Claims 45, 47, 54, 56, 62, 68, 78, 81, 88, 123-125 and 128 are rejected under 35 U.S.C. § 102(b) as being anticipated by Covacci *et al.* (*PNAS* 90: 5791-5795, June 1993 - Applicants' IDS).

The instant claims are not granted priority to the earlier application(s) because of the new matter currently included in the claims as explained above, but are granted the filing date of the

instant application.

Covacci *et al.* taught an isolated and purified immunogenic recombinant polypeptide of *Helicobacter pylori* comprising at least five, ten or fifteen contiguous amino acids from the instantly recited amino acids 750-977 of the amino acid sequence of SEQ ID NO: 5, wherein the polypeptide includes the amino sequence, EPIYA (SEQ ID NO: 10) or six contiguous amino acids, NNNNNN. The polypeptide is encoded by at least fifteen, thirty or forty-five contiguous nucleotides from nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO: 4. See Figures 2 and 3; Materials and Methods; and Results. The purified polypeptide is used to immunize rabbits (see page 5792, left column, last full paragraph; and the last two sentences in the paragraph bridging pages 5792 and 5793), and therefore is inherently contained in a pharmaceutically acceptable carrier and is inherently present in an immunologically effective amount. Covacci's polypeptide purification and immunization processes inherently involve the step of bringing into association the purified polypeptide with a pharmaceutically acceptable carrier.

Claims 45, 47, 54, 56, 62, 68, 78, 81, 88, 123-126 and 128 are anticipated by Covacci *et al.*

21) Claims 57, 59, 70 and 80 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Figura *et al.* (US 5,900,372, filed 10/16/1992) ('372) as evidenced by Figura *et al.* (US 5,866,375) ('375).

It is noted that unlike claim 63, the polypeptide comprising the recited number of amino acids of SEQ ID NO: 5 as claimed in claims 57, 59, 70 and 80, is neither required to be purified, nor isolated.

Figura *et al.* ('372) disclosed a composition comprising bacterial cells and a bacterial cell layer extracted from the CCUG 17874 cytotoxic strain of *H. pylori* contained in phosphate buffer (i.e., pharmaceutically acceptable carrier), which comprise the 130 kD cytotoxic and vacuolating protein as well as other proteins of *H. pylori*. A method of bringing the bacterial cells or the cell layer preparation into association with a buffer is taught, which method inherently involves the combining of cytotoxin or HSP to vacuolating potein, since the bacterial cells and the cell layer preparation of the *H. pylori* strain CCUG 17874 are expected to contain all these proteins. See Example 3, lines 7-9; and the second full paragraph in column 2; and Figures 1 and 2. That the prior art 130 kD protein is the 128 kD cytotoxin-associated protein and the 90 kD protein is the

immunoprotective VacA protein is inherent from the teachings of Figura *et al.* in light of what is known in the art. For instance, Figura *et al.* ('375) described these proteins as such. See column 2, first full paragraph; Figures 1, 2 and 4, and their descriptions; first paragraph of Examples 3 and 7; Examples 8 and 9; and claims. Although Figura *et al.* ('372) are silent about the SEQ ID number(s) as recited, since the prior art polypeptides produced by the same CCUG 17874 strain of *H. pylori* as that of Applicants' strain (see sections 'Materials and methods' and 'Results' of the instant specification), the prior art composition is expected to have the same structure as recited, absent evidence to the contrary.

The limitation 'recombinant' in the instant claims is viewed as a process limitation in product claims. It should be noted that when claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the isolation process results in a product that is structurally different from the product of the prior art.

Claims 57, 59, 70 and 80 are anticipated by Figura *et al.* ('372). The reference of Figura *et al.* ('375) is **not** used as a secondary reference in combination with Figura *et al.* ('372), but rather is used to show that every element of the claimed subject matter is disclosed by Figura *et al.* ('372). See *In re Samour* 197 USPQ 1 (CCPA 1978).

Rejection(s) under 35 U.S.C. § 103

22) Claim 63 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924) and Dunn *et al.* (*Infect. Immun.* 60: 1946-1951, May 1992 - Applicants' IDS) or Evans *et al.* (*Infect. Immun.* 60: 2125-2127, May 1992 - Applicants' IDS) in view of Hirschl *et al.* (*Eur. J. Clin. Microbiol. Infect. Dis.* 7: 100-105, 1988).

Cover *et al.* ('924) disclosed a method of bringing a purified 120-128 kilodalton polypeptide

into association with a pharmaceutically acceptable carrier. Cover's ('924) polypeptide comprises at least ten contiguous amino acids of the instantly recited amino acid sequence of SEQ ID NO: 5 and recombinant fragments thereof. See abstract; paragraph bridging columns 3 and 4; and first two paragraphs in column 4. The prior art polypeptide comprises Glu Phe Lys Asn Gly Lys Asn Lys Asp Phe Ser Lys Val Thr Gln Ala Lys Ser Asp residues which constitutes an at least ten contiguous amino acid residue-long fragment of the instantly claimed SEQ ID NO: 5 (see columns 31 and 32 of the '924 patent) and includes the instantly recited SEQ ID NO: 9, i.e., EFKNGKNKDFSK. The purified polypeptide fragments are used, in immunogenically effective amounts, as vaccines along with a pharmaceutically acceptable carrier (see fifth full paragraph in column 3; and section 'Vaccines' in column 10). Thus, a method of bringing the polypeptide into association with a pharmaceutically acceptable carrier is inherently disclosed. See the sequence search report attached to the Office Action mailed 05/20/03; and columns 31 and 32 of the '924 patent.

The teachings of Cover *et al.* ('924) is disclosed *supra*, which do not disclose the step of adding a second polypeptide comprising at least ten contiguous amino acids of *H. pylori* heat shock protein having the amino acid sequence of SEQ ID NO: 6.

However, Dunn *et al.* taught an intrinsically immunogenic heat shock protein of *H. pylori* comprising at least ten contiguous amino acids, from position 2-34 of the instantly recited SEQ ID NO: 6, AKEIKFSDSARNLLFEGVRQLHDAVKVTMGFRG, which protein isolated and/or purified from the water extract of whole cells or culture supernatants (see Figure 2 and pages 1948-1950).

Similarly, Evans *et al.* taught a purified heat shock protein of *H. pylori* comprising an N-terminal sequence at least ten contiguous amino acids in length, AKEIKFSDSARNLLFEGVRQLHDAVKVTMGFRG, from position 2-34 of the instantly recited SEQ ID NO: 6 (see Table 1; and abstract). Evans' protein is long enough to be immunogenic.

Hirschl *et al.* taught a highly purified *H. pylori* protein antigen with a molecular weight of approximately 120 kDa (see paragraph bridging pages 143 and 144 and Table 3). Hirschl *et al.* taught 'unicomponent antigens' of *H. pylori* such as the 120 kDa protein and "multicomponent" purified antigens, such as, the acid-glycine extract. Hirschl *et al.* taught a purified urease antigen of *H. pylori*. Hirschl *et al.* expressly taught mixing or combining various *H. pylori* antigens with the 120 kDa *H. pylori* antigen for use in serodiagnostic tests such as ELISA (see page 144; page 142 and

Tables 3 and 4).

Given Hirschl's express teaching of combining or mixing various *H. pylori* antigens, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Evans' or Dunn's intrinsically immunogenic heat shock protein of *H. pylori* to Cover's ('924) composition and thus provide the step of adding the *H. pylori* heat shock protein in Cover's ('924) method to produce the instant invention with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a method of producing a multicomponent antigen composition for use in serodiagnostic tests to diagnose *H. pylori* infections as taught by Hirsch *et al.*

Claim 63 is *prima facie* obvious over the prior art of record.

23) Claim 140 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924) and Cover *et al.* (US 6,054,132, filed 02/26/1992) ('132) in view of Hirschl *et al.* (*Eur. J. Clin. Microbiol. Infect. Dis.* 7: 100-105, 1988).

Cover *et al.* ('924) disclosed a method of bringing a purified 120-128 kilodalton polypeptide into association with a pharmaceutically acceptable carrier. Cover's ('924) polypeptide comprises at least ten contiguous amino acids of the instantly recited amino acid sequence of SEQ ID NO: 5 and recombinant fragments thereof. See abstract; paragraph bridging columns 3 and 4; and first two paragraphs in column 4. The prior art polypeptide comprises Glu Phe Lys Asn Gly Lys Asn Lys Asp Phe Ser Lys Val Thr Gln Ala Lys Ser Asp residues which constitutes an at least ten contiguous amino acid residue-long fragment of the instantly claimed SEQ ID NO: 5 (see columns 31 and 32 of the '924 patent) and includes the instantly recited SEQ ID NO: 9, i.e., EFKNGKNKDFSK. The purified polypeptide fragments are used, in immunogenically effective amounts, as vaccines along with a pharmaceutically acceptable carrier (see fifth full paragraph in column 3; and section 'Vaccines' in column 10). Thus, a method of bringing the polypeptide into association with a pharmaceutically acceptable carrier is disclosed. See the sequence search report attached to the Office Action mailed 05/20/03; and columns 31 and 32 of the '924 patent.

The teachings of Cover *et al.* ('924) is disclosed *supra*, which do not disclose the step of adding a second polypeptide comprising at least ten contiguous amino acids of *H. pylori* heat shock protein having the amino acid sequence of SEQ ID NO: 3.

However, Cover *et al.* ('132) taught a purified, immunogenic, recombinantly produced polypeptide of *H. pylori* comprising 23 contiguous amino acids, AFFTTVIIPAIVGGIATGTAVGT, of the instantly recited SEQ ID NO: 3 (see abstract; lines 29-47 of column 2; Example 2; Table 2 and SEQ ID NO: 13). The antigen is used for diagnostic purposes (see last paragraph in column 2).

Hirschl *et al.* taught a highly purified *H. pylori* protein antigen with a molecular weight of approximately 120 kDa (see paragraph bridging pages 143 and 144 and Table 3). Hirschl *et al.* taught 'unicomponent antigens' of *H. pylori* such as the 120 kDa protein and "multicomponent" purified antigens, such as, the acid-glycine extract. Hirschl *et al.* taught a purified urease antigen of *H. pylori*. Hirschl *et al.* expressly taught mixing or combining various *H. pylori* antigens with the 120 kDa *H. pylori* antigen for use in serodiagnostic tests such as ELISA (see page 144; page 142 and Tables 3 and 4).

Given Hirschl's express teaching of combining or mixing various *H. pylori* antigens, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Cover's ('132) immunogenic polypeptide of *H. pylori* to Cover's ('924) composition and thus provide the step of adding Cover's ('132) immunogenic polypeptide in Cover's ('924) method to produce the instant invention with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a method of producing a multicomponent antigen composition for use in serodiagnostic tests to diagnose *H. pylori* infections as taught by Hirsch *et al.*

Claim 140 is *prima facie* obvious over the prior art of record.

Remarks

24) Claims 45, 47, 54, 56, 57, 59, 62, 63, 68, 70, 78, 80, 81, 88, 123-126, 128 and 140 stand rejected. Claims 40, 41, and 127 are allowable.

25) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

26) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER

SEQ ID NO. 4 & 5
Fragment

PD 04-APR-1995.
XX
PF 26-APR-1993; 93US-00053614.
XX
PR 13-OCT-1992; 92US-00959940.
XX
PA (UYVA-) UNIV VANDERBILT.
XX
PI Blaser MJ, Tummuru MKR, Cover TL;
XX
DR WPI; 1995-146855/19.
DR N-PSDB; AAQ86728.
XX
PT New nucleic acid encoding tag A antigen of Helicobacter pylori - used to
PT detect predisposition to peptic ulceration and to produce protein for use
PT in vaccines, diagnosis etc.
XX
PS Disclosure; Col 37-46; 30pp; English.
XX
CC The full-length sequence of the tagA gene of H. pylori 84-183 (ATCC
CC 53726) was obtained from overlapping clones isolated from genomic
CC libraries. The gene encoded a 1181-amino acid TagA antigen protein
CC (AAR72593) and a truncated antigen (AAR72594). (Updated on 25-MAR-2003 to
CC correct PF field.)
XX
SQ Sequence 859 AA;

Alignment Scores:

Pred. No.:	4.21e-14	Length:	859
Score:	25.00	Matches:	25
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	10.96%	Indels:	0
DB:	2	Gaps:	0

US-09-360-685B-4_COPY_2782_3466 (1-685) x AAR72594 (1-859)

```
Qy        160 GTAGAGCAAGCGTTAGCCGATCTCAAAAATTTCTCAAAGGAGCAATTGGCCCAACAAGCT 219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        803 ValGluGlnAlaLeuAlaAspLeuLysAsnPheSerLysGluGlnLeuAlaGlnGlnAla 822

Qy        220 CAAAAAAATGAAAGT 234
              |||||||||||||||
Db        823 GlnLysAsnGluSer 827
```

RESULT 7
JQ1320
high mobility group protein Pf16 - malaria parasite (Plasmodium falciparum)
C;Species: Plasmodium falciparum
C;Date: 31-Mar-1992 #sequence_revision 31-Mar-1992 #text_change 09-Jun-2000
C;Accession: JQ1320
R;Guntaka, R.V.; Kandala, J.C.; Reddy, V.D.
Biochem. Biophys. Res. Commun. 182, 412-419, 1992
A;Title: Cloning and characterization of a highly conserved HMG-like protein (PF16) gene
A;Reference number: JQ1320; MUID:92118046; PMID:1731798
A;Accession: JQ1320
A;Molecule type: DNA
A;Residues: 1-147 <GUN>
A;Cross-references: GB:M86518; NID:g160325; PID:g160326
A;Experimental source: strain FCR/3
C;Comment: This protein interacts with other nuclear proteins and serve as a transcripti
C;Genetics:
A;Gene: pf16
F;7-18,19-30/Region: duplication
F;70-91/Region: aspartic acid/glutamic acid-rich
F;126-133/Region: basic

NNNNN

Alignment Scores:

Pred. No.:	38.7	Length:	147
Score:	8.00	Matches:	8
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	3.51%	Indels:	0
DB:	2	Gaps:	0

US-09-360-685B-4_COPY_2782_3466 (1-685) x JQ1320 (1-147)

```
Qy        391 AATAACAATAACAATAATGGACTC 414
              ||||||||||||||||||||||||
Db         94 AsnAsnAsnAsnAsnAsnGlyLeu 101
```